

Modern Concepts of Cardiovascular Disease

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THE EFFECTS OF THE ADMINISTRATION OF CORTISONE AND ACTH ON PATIENTS WITH ACUTE RHEUMATIC FEVER

Hench, Kendall, Slocumb and Polley studied the effects of the administration of cortisone and ACTH on patients suffering from rheumatoid arthritis. Their preliminary report indicated a rapid clinical improvement in these patients. Since the pathologic processes in rheumatoid arthritis and rheumatic fever manifest themselves in collagenous tissue, it seemed logical to observe the effects of cortisone and ACTH on patients with rheumatic fever.

The first observation of the effects of cortisone on rheumatic fever was made on a girl, 15 years of age, who was admitted to the hospital March 26, 1949, in her first attack of this disease. At 7 p.m. on March 28, the first injection of 100 mg. of cortisone was given. During the next ten days 100 mg. of cortisone were administered twice daily. The daily dose was 100 mg. from April 8 to 19 inclusive; 50 mg. from April 20 to 22; 100 mg. from April 23 to May 4 and none thereafter.

The fever disappeared in three days after administration of cortisone was started; exquisitely tender joints became free of symptoms in three and a half days; the heart rate dropped from 122 to 60 beats per minute in three and a half days; the P-R interval in the electrocardiogram decreased from 0.24 to 0.16 second in eight and a half days and the sedimentation rate dropped from 114 to 17 mm. in one hour (Westergren method) after nineteen days. The hemoglobin which was 12.9 gm. at the initial examination increased to 14.0 gm. five days before administration of cortisone was discontinued. The albumin-globulin ratio rose from an initial value of 1.14 to 1.7 five days before use of cortisone was discontinued. This change represented a moderate increase in the albumin fraction and a decrease in the globulin component.

On April 22 the sedimentation rate increased in spite of increasing the dose of cortisone from 50 to 100 mg. daily. Careful studies on the blood at that time indicated that the patient had mild infectious mono-

nucleosis, but there was no exacerbation of articular symptoms, there was no fever and the patient felt well. The sedimentation rate continued to rise during the next several weeks reaching a peak of 74 mm. in one hour on June 3 after which it declined to 26 mm. in one hour on June 30 without further therapy.

During the time the patient was under observation a soft diastolic murmur was heard intermittently over the third intercostal space to the left of the sternum. Its character was never such that any conclusion could be reached as to its significance. The patient was dismissed from the hospital in good condition July 2, two months and seven days after admission.

She was re-examined July 28, 1949, at which time she felt well and was moderately active. There was no elevation of temperature and the sedimentation rate was 17 mm. in one hour. The P-R interval was 0.14 second and no abnormalities were detected on physical examination of the heart. Similar re-examinations have been carried out at intervals of approximately a month to the present. These examinations have revealed no cardiac abnormalities, the sedimentation rates have been of normal values and the P-R intervals have been within the range of normal. The patient is active and attending school.

The effects of cortisone have been observed on 4 more patients with acute rheumatic fever. Some of these patients had had rheumatic fever previously and had valvular damage with or without cardiac enlargement. The effects of the administration of ACTH have been observed on an additional 4 patients with acute rheumatic fever.

Summary of the Clinical Effects of Cortisone

After the administration of cortisone was begun, fever disappeared in from one to twelve days, articular symptoms were abolished in three to six days, the sedimentation rate returned to normal in from twelve to

nineteen days, the heart rate returned to normal in from two to six days (except in 2 patients considered to have rheumatic myocarditis) and, as a rule, the accelerated heart rate was succeeded in a few days by bradycardia with rates of less than 50 per minute. In each instance the bradycardia disappeared completely either when the dose of cortisone was reduced or discontinued. Prolonged P-R intervals became normal in approximately eight days except in 1 case in which there was previous severe organic heart disease with aortic regurgitation. In this case the P-R interval fell from 0.26 to 0.22 second. In each of the 5 cases the albumin-globulin ratio rose sharply while the patients were receiving cortisone.

Evidence of Recurrent Activity of the Rheumatic Process—In the first patient a rise in the sedimentation rate occurred while the patient was receiving a reduced dose of cortisone (50 mg. daily), and the sedimentation rate continued to rise in spite of increasing the dose to 100 mg. daily. This was accounted for by an attack of infectious mononucleosis. The episode was not attended by any evidence of reactivation of the rheumatic process.

In a second case manifestations of rheumatic activity occurred after the administration of cortisone was discontinued. Resumption of use of cortisone abolished the evidence of rheumatic activity though less promptly than at its first administration.

In a third case the sedimentation rate rose moderately, and there was a distinct increase in the pulse rate although the patient remained afebrile and had no joint manifestations after administration of cortisone was discontinued.

In the fourth case the sedimentation rate did not rise after administration of cortisone was discontinued nor were there other evidences of recurrence of an active rheumatic process.

Clinical Effects of ACTH

The effects of the administration of ACTH on 4 patients who had acute rheumatic fever have paralleled closely those described for patients receiving cortisone.

Side-effects of the Administration of Cortisone and ACTH

In general, the patients tended to gain weight rapidly. A moon-shaped facies devel-

oped frequently, and occasionally there was stimulation of growth of hair on the face. Any previous tendency to acne vulgaris was accentuated. Striae over the buttocks developed in several patients. Menstruation when established was temporarily suppressed. All these manifestations abated after administration of these drugs had been discontinued for several weeks.

Results of Re-examination of Patients After Dismissal From the Hospital and Comment

Results of re-examination of these patients over a period of eight to ten months following the first administration of cortisone or ACTH may be summarized as follows:

1. Those patients having murmurs considered to be due to an old endocarditis from previous attacks of rheumatic fever have exhibited no change in the murmurs.

2. Patients admitted in their first attack of rheumatic fever have presented, to date, no significant evidence of organic involvement of the endocardium, have had no recurrence of rheumatic activity and are without evidence of cardiac enlargement.

One of the patients who received cortisone and was considered to have myocarditis at the time of admission has resumed moderate activities in school without evidence of myocardial insufficiency.

A patient currently receiving cortisone was admitted with evidence of myocarditis consisting of pericarditis, pulmonary congestion with pleural effusion and a probable rheumatic pleuritis together with cyanosis and dyspnea requiring the administration of oxygen. These signs and symptoms disappeared approximately two weeks after administration of cortisone was started.

Continued observation of these patients will be required before it can be determined whether cortisone or ACTH prevents the development of chronic heart disease following an attack of acute rheumatic fever or its aggravation in hearts previously damaged by this disease. Up to now the results in this respect are quite encouraging.

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INSTRUCTIONS FOR PRESENTATION OF PAPERS

1. American Heart Association. 300-word abstract (in triplicate) to be submitted to Doctor Louis E. Martin, 1136 West Sixth Street, Los Angeles 14, California, by March 1, 1950.
2. International Cardiological Congress. 300-word abstract (in triplicate) to Doctor Charles A. R. Connor, American Heart Association, 1775 Broadway, New York 19, N. Y., by March 1, 1950.

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